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— *of inventorship (Rule 4.17(iv)) for US only*

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(54) Title: A NOVEL AMORPHOUS FORM OF VALSARTAN

(57) Abstract: The present invention relates to a novel amorphous form of valsartan, to a process for its preparation and to a pharmaceutical composition containing it.

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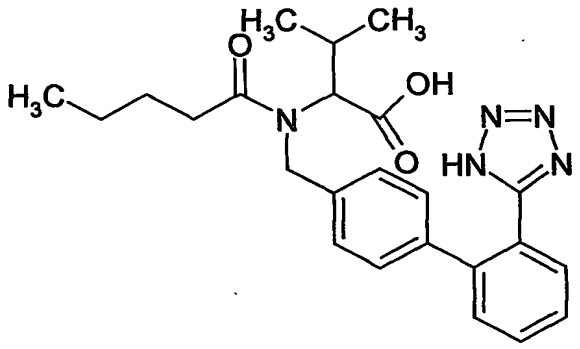
A NOVEL AMORPHOUS FORM OF VALSARTAN

FIELD OF THE INVENTION

The present invention relates to a novel amorphous form of valsartan, to a process for its preparation and to a pharmaceutical composition containing it.

BACKGROUND OF THE INVENTION

Valsartan of formula (1):



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or N-(1-Oxopentyl)-N-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-L-valine, is an antihypertensive agent and its therapeutic uses are disclosed in US 5,399,578. No polymorphs of valsartan is reported in the literature.

We discovered a sufficiently stable amorphous form of valsartan, which is found to be suitable for pharmaceutical composition.

The object of the present invention is to provide a novel stable amorphous form of valsartan, process the preparing it and a pharmaceutical composition containing it.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides a novel amorphous form of valsartan (hereinafter referred to as amorphous valsartan). The amorphous valsartan is characterized by having broad x-ray diffraction spectrum as in figure 1.

A further aspect of the present invention provides a process for the preparation of amorphous valsartan. Amorphous valsartan is prepared by dissolving valsartan in an alcohol or a mixture of alcohols. The alcohol is selected from the group consisting of methanol, ethanol, isopropyl alcohol, tert-butyl alcohol and n-butyl alcohol. The solvent may be removed from the solution by vacuum drying or spray drying.

A further aspect of the present invention provides a pharmaceutical composition comprising amorphous valsartan and a pharmaceutically acceptable carrier.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a x-ray powder diffraction spectrum of amorphous valsartan.

x-Ray powder diffraction spectrum was measured on a Siemens D5000 x-ray powder diffractometer having a copper-Kα radiation.

The following examples further illustrate the invention.

Example 1

Valsartan (10 gm), (obtained by the process described in example-16 of US 5,399,578) is dissolved in methanol (50 ml). The solution is subjected to vacuum drying at about 40^{0}C for 10 hours to give 9.8 gm of amorphous valsartan.

Example 2

Example 1 is repeated by subjecting the solution to spray drying instead of vacuum drying to give amorphous valsartan.

Example 3

Valsartan (10 gm), (obtained by the process described in example-16 of US 5,399,578) is dissolved in ethanol (60 ml). The solution is subjected to vacuum drying at about 45^{0}C for 12 hours to give 9.7 gm of amorphous valsartan.

Example 4

Example 3 is repeated by subjecting the solution to spray drying instead of vacuum drying to give amorphous valsartan.

Example 5

Valsartan (10 gm) is dissolved in isopropyl alcohol (70 ml). The solution is subjected to vacuum drying at about 45^{0}C for 15 hours to give 9.9 gm of amorphous valsartan.

We claim:

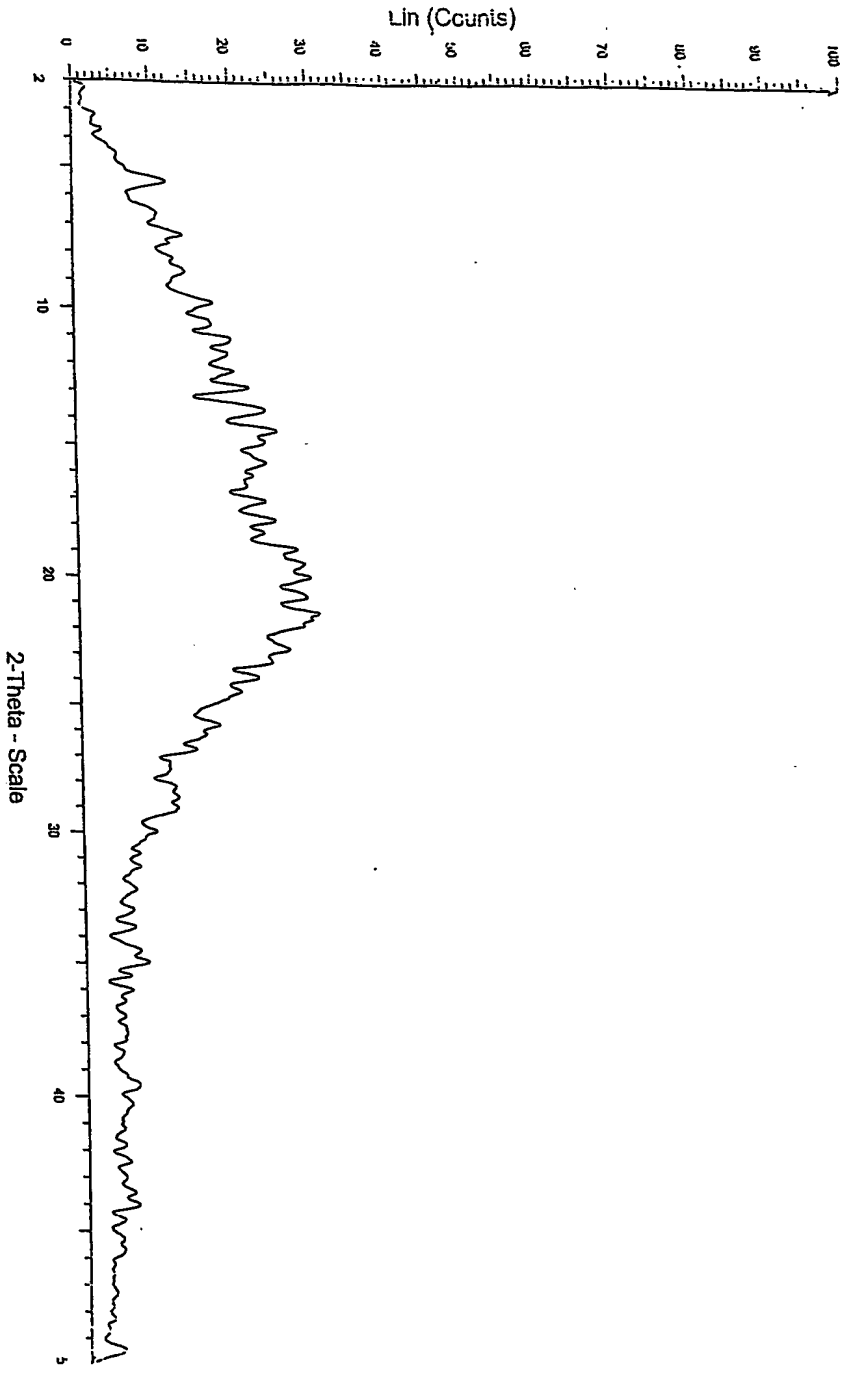
1. Amorphous valsartan characterized by an x-ray powder diffraction spectrum as in figure 1.
2. A process for preparation of amorphous valsartan of claim 1, which comprises:

a) dissolving valsartan in an alcohol or a mixture of alcohols;

b) removing the solvents from the solution formed in step (a) either by vacuum drying or by spray drying;

wherein the alcohol is selected from the group consisting of methanol, ethanol isopropyl alcohol, tert-butyl alcohol and n-butyl alcohol.

3. A process according to claim 3, wherein the solvent is removed by vacuum drying.
4. A process according to claim 3, wherein the solvent is removed by spray drying.
5. A pharmaceutical composition comprising amorphous valsartan and a pharmaceutically acceptable carrier.


Lin (Counts)
0
10
20
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100
2
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5
2-Theta - Scale

INTERNATIONAL SEARCH REPORT

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CLASSIFICATION OF SUBJECT MATTER

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

REGISTRY, CAPLUS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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A	CN 1317485 A (Pharmaceutical Co., Ltd., Changzhou Pharmaceutical Factory No.4, Peop. Rep. China) 17 October 2001 (17.10.01) *abstract.*	1-5

☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

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Name and mailing adress of the ISA/AT Austrian Patent Office Dresdner Straße 87, A-1200 Vienna Facsimile No. 1/53424/535	Authorized officer MÜLLER-HIEL R. Telephone No. 1/53424/434

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Jia, Qingzhong; Ma, Guilin; Li, Wenzhi; Jiang, Shaohao "Synthesis of antihypertensive drug valsartan"Zhongguo Yiyao Gongye Zazhi (2001), 32(9), 385-387 CODEN: ZYGZEA; ISSN: 1001-8255 (abstract). Chemical Abstracts [online] Copyright 2003 American Chemical Society [retrieved on 12 August 2003 (12.08.03)]. Retrieved from STN International, Karlsruhe. Chem. Abstr. No. 2001:807594 CAPLUS; abstract. *abstract.*	1-5

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/IN 03/00096-0

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